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Preoperative Diagnosis of Carcinoma of the Breast: Is a "Cost-cutter" Algorithm Tenable?

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Background: Decision making in favor of conservative breast surgery is dependent upon the accuracy of preoperative evaluation of tumor stage, of which imaging modalities occupy a pivotal role. Systematic studies correlating the relative accuracy of various evaluating strategies are few, but remain vital means of making the optimal selection of diagnosis and subsequent treatment option. In this study, we evaluated the relative efficacy of: (1) palpation (P), (2) ultrasonography (US), and (3) bilateral mammography (MG) of the breast and axilla.

Methods: In a prospective study, 109 female patients undergoing a modified radical mastectomy were subjected to a preoperative diagnostic assessment protocol involving palpation, ultrasonography, and bilateral mammography of the breast and axilla. Subsequently the preoperative findings were correlated to the postoperative histopathological reports. Cancer-specific criteria evaluated were tumor size, location, histologic type, histoarchitecture, and calcification, as well as status of regional nodes. Patient-specific criteria included age, size, and density of the breast and presence of associated benign breast disease. Percentage sensitivity, specificity, and positive and negative predictive values were determined for MG, US, and P as well as MG + P and US + P.

Results: In assessment of the primary tumor, P, MG, and US showed an overall sensitivity of 88%, 92%, and 90%, respectively; MG + P and US + P had a sensitivity of 99% each. In nodal assessment, P, MG, and US showed an overall sensitivity of 88%, 69%, and 77%, respectively; MG + P and US + P had a sensitivity of 90% and 94%, respectively. Mammography understaged the tumor, whereas US and P overstaged tumors as well as nodes. US was particularly better than MG in younger women, smaller breast size, denser breast consistency, with or without associated benign breast disease, and cystic or necrotic tumors with invasive ductal histology. In addition, US was comparable to MG in most of the other criteria as well. Disadvantages of US over MG were its complete inability to detect microcalcification and certain intraductal cancers.

Conclusion: We conclude that: (1) the combination of US and P provides equivalent preoperative efficacy as MG, (2) the combination is more cost-effective preoperative assessment for subsequent selection of therapeutic modality, and (3) in certain well-defined circumstances discussed by us, mammography is most useful and should be considered as the imaging modality of choice. J. Surg. Oncol. 64:153–158

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INTRODUCTION

The efficacy of conservative surgery for breast cancer depends heavily on a sensitive preoperative diagnosis. Inaccurate assessment may lead to unjustifiable overtreatment or, in contrast, an increased risk of postoperative recurrence. Besides other criteria for selection of type of therapy, tumor size remains an important factor [1,2].

Palpation allows at best only a rough approximation of tumor size, especially in small tumors. In addition, the size, consistency, and associated benign breast disease affect the sensitivity further. Besides clinical palpation (P), mammography (MG) and breast sonography (US) have been useful adjuncts in detecting small and sometimes nonpalpable carcinomas [3–5]. Most patients tend to have both MG as well as US performed preoperatively. Although MG and US are considered mutually complementary, few systematic studies correlate the efficacy of P-, MG-, and US-determined tumor characteristics to histologic findings. Moreover, the few comparative studies that have been performed have assayed only tumor diameters and have not defined most criteria that determine the strength and limitations of each investigation [6,7].

The lifetime risk of developing breast cancer for women in the United States being 1:10 [8], every patient undergoing each investigation would add significantly to the financial burden of treatment. However, appropriate selection of the most effective investigation in the most appropriate patient means greater efficacy and, more important in the current setting, would mean lower costs.

Our study aims at defining: (1) the sensitivity of each individual preoperative modality by comparing their results to histologic findings, (2) the best combinations of investigations that would yield the highest efficacy, (3) tumor-specific and patient-specific criteria that enhance or diminish the sensitivity of each individual investigation, and (4) an algorithm for selection of the most effective investigation/s in the appropriate patient that would yield desired results, be cost effective, and less cumbersome to the patient. In achieving these mentioned above, our study is unique since it satisfies the following criteria: (1) the study population is modest, with an adequate representation of the various criteria evaluated, (2) every patient has undergone each of the investigations, thereby providing a strong basis for comparison of each modality, and (3) other criteria determining individual sensitivities of each modality have been evaluated in the same study population.

MATERIALS AND METHODS

A total of 109 patients scheduled for modified radical mastectomy, per primum, for histologically proven breast cancer were included in this prospective study. Patients with recurrence or those who had received anticancer therapy earlier were excluded. All our patients were females between the ages of 23 and 69 years. Eighteen patients had pT1 lesions, 50 had pT2, 32 had pT3, and 9 had pT4 tumors. Patients with pT4 lesions ($n = 9$) underwent a radical mastectomy ($n = 4$) or partial excision of pectoralis major muscle ($n = 5$). Clinical data were compiled and findings pertaining to the site, size of primary tumor, and details of axillary nodes and clinical TNM stage were recorded. Every patient underwent a preoperative ultrasonography (US) using a ultrasound probe (7.5 MHz) followed by a mammography (MG). Clinical, sonographic, and mammographic reports were compared to histopathological findings and the pTNM stage. Criteria evaluated for possible correlation included: (1) tumor-specific data, such as tumor size, location, histologic type, histoarchitecture, and calcification as well as status of axillary nodes, and (2) patient-specific criteria including age, size and density of the breast, and presence of associated benign breast disease. Percentage sensitivity, specificity, positive, and negative predictive values were determined individually for MG, US, and P, as well as for combinations of the preoperative modalities under evaluation, i.e., MG + P and US + P.

RESULTS

The overall sensitivity of the preoperative diagnostic methods used for the primary tumor and axillary nodes is summarized in Figure 1 and Table I, respectively. In the assessment of the primary tumor, US + P is as sensitive as MG + P, whereas US is slightly more sensitive than MG alone. In nodal assessment, palpation alone is very sensitive, whereas US alone is far superior than MG. The sensitivity of US is greatly enhanced when assessed in conjunction with palpation.

The variation in accuracy in relation to certain tumor-specific, organ-specific, and patient-specific criteria is summarized in Tables II, III, and IV, respectively. Additionally each table enlists the recommended investigation, based upon the highest sensitivity values, thereby forming an algorithm for investigational approach. The results show that US is better in assessment of invasive tumors located in any quadrant, especially if they are cystic and necrotic. MG is less sensitive at detecting tumors involving the upper inner quadrant and more efficient than US with intraductal lesions. US is virtually blind to calcification, whereas M is exquisitely sensitive to it. US is uniformly sensitive in the assessment of breast tumors irrespective of the patients' age, size of breast, and consistency of breast tissue. MG is less sensitive than US in detecting cancers in younger women, or women with smaller breasts with a dense cellularity. Logically in these patients, US is more valuable, as seen

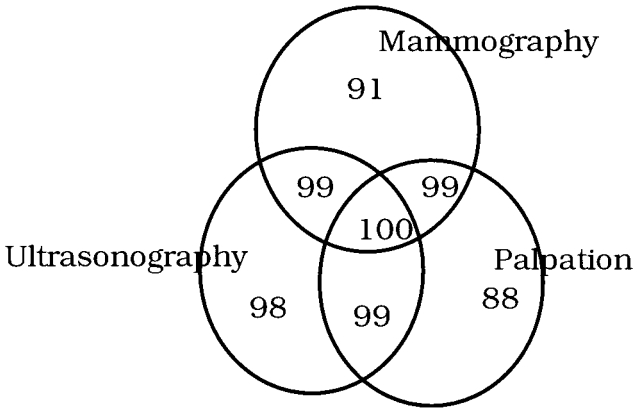

Fig. 1. Preoperative diagnosis of primary tumor: percentage sensitivity of mammography, ultrasonography, palpation and combinations thereof.

in Table III. US is slightly better than M in detecting lesions in patients with associated benign breast disease.

Comparative assessment of size of the primary tumor by the three methods is correlated with actual histologic mean tumor diameter as shown in Figure 2. Ultrasonography and palpation significantly overstage the tumor size, whereas M actually understages the lesions. In summary, US is as sensitive as MG in detection of breast tumors, as regards most of the criteria we have evaluated, US is able to detect tumors in certain situations where MG is less effective, and US satisfies a wider range of criteria than MG in the preoperative diagnosis.

DISCUSSION

Mammography and breast sonography have been found to be mutually complementary adjuncts to preop-

TABLE I. Carcinoma of the Breast: Overall Efficacy in Preoperative Diagnosis of *Axillary Nodal Metastasis*

	% Sensitivity	% Specificity	PPV %	NPV %
Mammography (M)	69	67	86	43
Ultrasonography (US)	77	71	88	52
Palpation (P)	88	85	94	72
M + P	90	86	95	76
US + P	94	90	98	82

TABLE II. Comparison of Mammography (M), Ultrasonography (US), and Palpation (P) with Histological Examination: *Tumor-Specific Criteria*

	Percentage accuracy				Algorithm*
	M (n=)	US (n=)	P (n=)	Histology n=	Recommended investigation
Tumor size					
• T1	94 (17)	94 (17)	77 (14)	18	MG/US
• T2	88 (44)	92 (46)	86 (43)	50	US
• T3	93 (29)	90 (28)	93 (29)	32	MG/US
• T4	100 (9)	100 (9)	100 (9)	9	MG/US
Calcification					
• Present	99 (67)	21 (14)	—	68	MG
• Absent	90 (37)	—	—	41	MG/US
Tumor location					
• Upper Inner	94 (18)	100 (21)	100 (21)	21	US
• Upper Outer	100	100	100	31	MG/US
• Lower Inner	100	100	100	32	MG/US
• Lower Outer	100	100	100	20	MG/US
• Central	100	100	100	5	MG/US
Tumor histology					
• Intraductal	95 (20)	57 (12)	61 (13)	21	MG
• Invasive ductal	94 (69)	97 (71)	94 (69)	74	MG/US
• Lobular	66 (4)	100 (6)	100 (6)	6	US
• Other	75 (6)	100 (8)	87 (7)	8	US
Histoarchitecture of the tumor					
• Hyperplastic	96 (49)	100	50 (25)	50	MG/US
• Fibrotic	66 (20)	93 (28)	93 (28)	30	US
• Necrotic	85 (12)	100	42 (6)	14	US
• Cystic	80 (12)	100	26 (4)	15	US

*Algorithm: 1. US is recommended for T1 & T2 tumors, in the upper inner quadrant, especially with lobular pathology. 2. MG is best for detection of T1, T3 and T4 tumors with associated calcific changes.
n = number of patients.

TABLE III. Comparison of Mammography (M), Ultrasonography (US), and Palpation (P) as Confirmed Histological Examination with Respect to *Organ-specific Criteria*

	Percentage accuracy			Algorithm*
	M (n=)	US (n=)	P (n=)	Recommended investigation
Size of breast				
• Small (n = 41)	80 (33)	92 (38)	85 (35)	US
• Medium (n = 42)	93 (39)	95 (40)	95 (40)	MG/US
• Large (n = 26)	96 (25)	92 (24)	92 (24)	MG/US
Density of breast tissue				
• Dense (n = 58)	83 (48)	93 (54)	91 (53)	US
• Fatty (n = 51)	92 (47)	96 (49)	90 (46)	MG/US
Associated pathology in surrounding breast				
• None (n = 60)	86 (51)	87 (52)	87 (52)	MG/US
• Mastitic (n = 32)	81 (26)	93 (29)	78 (25)	US
• Fibrocystic (n = 17)	70 (12)	88 (15)	59 (10)	US

*Algorithm: 1. US is recommended for smaller tumors, denser consistency, associated with fibrocystic mastitis. 2. MG is best for detection of medium or larger tumors with fatty density.
n = number of patients.

TABLE IV. Percentage Accuracy of Mammography (M), Ultrasonography (US), and Palpation (P): *Patient-specific Criteria*

	Percentage accuracy			Algorithm*
	M (n=)	US (n=)	P (n=)	Recommended investigation
Axillary nodes				
N0 (20)	67 (13)	71 (14)	85 (17)	P
N1 (58)	47 (27)	77 (45)	88 (51)	P/US
N2 (31)	76 (23)	76 (23)	84 (26)	P/US
Age in years (n)				
<35 (28)	82 (23)	93 (26)	90 (25)	US
35–50 (42)	93 (39)	92 (38)	93 (39)	MG/US
>50 (39)	94 (37)	90 (35)	93 (36)	MG/US

*Algorithm: 1. Palpation is accurate in axillary assessment wherein US is the second choice. 2. US is best for detection of tumors in younger women whereas MG is preferred in women >35 years of age.
n = number of patients.

erative clinical examination by most studies [9–12] However, in the setting of most developing countries, where diagnostic armamentarium is sparingly available, it is more important to optimize their use. In some studies by Eohnosu et al [13] US was able to detect tumors in all cases regardless of tumor size whereas MG detected T2 size tumors in 64.7% of cases only. Ciatto et al. [11] showed that US sensitivity was unaffected by age yet strongly influenced by tumor size (pT1, 76%; pT2, 87%) and histologic type (intraductal, 7.4%; invasive/ductal lobar, 83.4%; invasive special types, 64.1%). Our study shows that US is effective irrespective of age and tumor size.

In most studies the features of the lesions at US associated with cancer (irregular margins, posterior acoustic shadowing) or benign lesions (anechoic structure, lateral shadowing, posterior acoustic enhancement) have been exactly similar to the criteria of diagnosis used in our study. The increased sensitivity of US is based largely on the following sonographic criteria as have been defined by Venta et al. [14]. 5–10 MHz linear transducers are essential with the imaging within the transducer focal zone associated with relatively steep time-grain compensation curves. Sonographically fat in the normal breast tissue is hypoechoic, fibrous tissue is echogenic, and glandular tissue is of intermediate echogenicity. False positives may result due to the evaluation of the following structures: (1) anterior costochondral junction imaged in cross section and (2) fat lobules outlined by Cooper ligaments when imaged in a perpendicular plane.

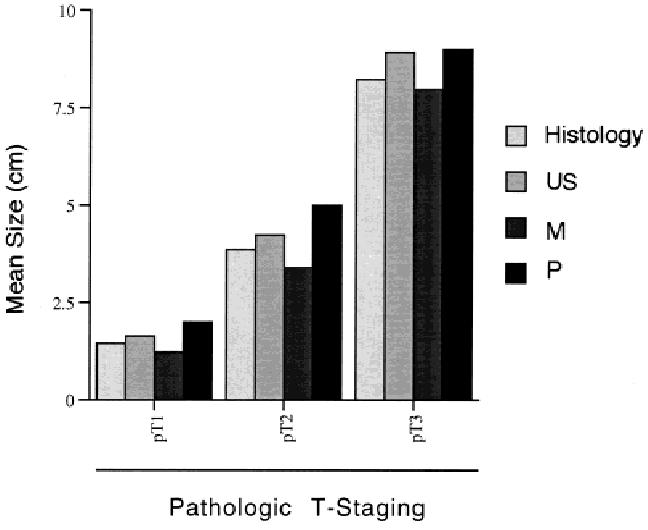

Fig. 2. Comparison of mean tumor diameter (cm) as determined by histology, ultrasonography (US), mammography (M), and palpation (P).

Typically cysts are anechoic with sharp margins and show posterior acoustic enhancement, whereas benign solid lesions are hypoechoic with variable sonographic appearance. Carcinoma of the breast presents as a sonographically hypoechoic mass with heterogeneous internal echoes, irregular margins and variable acoustic shadowing, although occasionally some malignant tumors may appear well circumscribed and show posterior acoustic shadowing. Breast sonography proves to be the most efficient for women <40 years [15,16], in patients with dense breasts and in distinguishing between cystic and solid tumors [4,17].

Eohnosu et al. [13] found CT to be most sensitive to nodal metastasis followed by US. US was superior to MG, CT, and DSA for detecting primary tumors, but CT was better than US for evaluation of axillary nodes. In our study, US was second to palpation in detection of axillary nodes. In inconclusive cases, US guided nodal aspiration and cytology may reduce the frequency of unnecessary nodal biopsies as well.

In studies by Lauth et al. [18] and Strasser et al. [4], mammography has been found to be extremely sensitive in the diagnosis of small carcinomas (<1 cm) with a sensitivity ranging from 91–93% for mammography to only 54–76% for sonography. A larger discrepancy between these two methods was described by Rosner and Blaird [19] in which all tumors <1 cm were detected by mammography, whereas only 25% were detected by sonography. In our study, there were only nine patients with tumors < 1 cm diameter; hence no strong conclusions could be drawn.

Conceivably, the false negative results in the sonographic investigations of tumors <1 cm is the sonographic blindness to microcalcification [15,16] In our evaluation of tumor-specific criteria as well, calcification remained largely undetected by US, whereas MG was very sensitive.

''Calcification-blindness'' and associated false negativity in small tumors makes sonography unsuitable for breast screening, as corroborated by many reports [4,15,16].

In investigations by Meden et al. [10], the preoperative determination of carcinoma size concurred with the histometrically determined tumor stages in 71.5% of cases by mammography, 77% by sonography, and 58% by clinical examination. These results are comparable with those obtained by Fornage et al. [6]. Our study shows similar distribution and also confirms that MG, P, and US understage (MG) or overstage (P or US) the actual tumor size.

CONCLUSION

Based on these findings, we propose an algorithm for preoperative assessment of breast tumors:

1. For tumors <1 cm, or barely palpable tumors, or patients with intraductal lesions, MG is essential.
2. In all other patients, US is effective, with the sensitivity enhanced when US is interpreted with palpation.
3. US is particularly more useful in women with smaller breast size, associated benign breast disease, age <35 years, and with invasive ductal pathology.
4. Detection of axillary nodes is best performed by palpation followed by US.

We believe that following this algorithm would result in a cost-effective and less laborious investigational approach to the management of breast tumors.

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